

WHAT IS CLAIMED IS:

1. A method of identifying a high-affinity interacting domain in a chosen protein, domain thereof or part thereof and the amino acid sequence thereof comprising:
 - 5 a) providing a set of overlapping peptides spanning a complete sequence of said chosen protein, domain thereof or part thereof, covalently bound to a support;
 - b) providing a mixture of proteins and/or a mixture of peptides;
 - c) incubating said set of overlapping peptides of a), with said mixture of b), under conditions enabling the binding between a high-affinity interacting domain in a peptide of
 - 10 said set and one or more protein or peptide of b) to occur;
 - d) washing of any protein-protein interaction which is not a high-affinity interaction of c); and
 - e) identifying which peptide of a) interacts with high-affinity to a protein or peptide of b), thereby identifying said peptide of e) and the sequence thereof as a high-affinity interacting domain.
- 15 2. The method of claim 1, wherein said mixture of proteins and/or mixture of peptides contains a label.
3. The method of claim 1 or 2, wherein said set of overlapping peptides is
- 20 synthesized synthetically using the sequence of said chosen protein.
4. The method of claim 1, 2 or 3, wherein said support is chosen from a chip, a bead, or a plate.
- 25 5. A method of identifying an agent which modulates an interaction between high-affinity interacting domains between a set of overlapping peptides spanning a complete

sequence of a chosen protein, domain thereof or part thereof, covalently bound to a support and a mixture of proteins and/or a mixture of peptides comprising:

a) incubating said set of overlapping peptides, with said mixture in a presence of at least one agent, under conditions enabling the binding between a high-affinity interacting domain

5 in a peptide of said set and one or more protein or peptide of said mixture to occur;

b) washing of any protein-protein interaction which is not a high-affinity interaction of b); and

c) identifying which peptide of a) interacts with high-affinity to a protein or peptide of said mixture in a presence of said agent as compared to in an absence thereof,

10 thereby identifying said agent as a modulator of said high-affinity interaction when said interaction in the presence of said agent is measurably different from in the absence thereof.

6. The method of claim 5, wherein said mixture of proteins and/or mixture of
15 peptides contains a label.

7. The method of claim 5 or 6, wherein said set of overlapping peptides is synthesized synthetically using the sequence of said chosen protein.

20 8. The method of claim 5, 6 or 7, wherein said support is chosen from a chip, a bead, or a plate.

9. A modulator of high-affinity interaction identified by any one of said method of claims 5-9.

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